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THE THERAPEUTIC PROPERTIES OF ANIMAL EXTRACTS.[1]

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Gentlemen:—In connection with the treatment by hypodermatic injections of an extract of the pancreas, of a case of diabetes in the wards, and in connection with the treatment by dessicated thyroid gland of some cases of circulatory disorder in patients attending the dispensary, it has been suggested that I should discuss with you the general subject of the use of animal extracts in the treatment of disease. This, as you are aware, is by no means a new therapeutic method; it descends from the fathers of medicine; by whom, I mean not Hippocrates and Galen, but the shamans, the wizards, and the obi-men of savage tribes.

Western medicine has progressed beyond the stage of witchcraft, but even to-day, in China and other eastern lands, the viscera of animals and the bodies of reptiles are favorite medicinal preparations. You may be familiar with one of Sir Edwin Arnold's poems of Japan, which turns upon the necessity of obtaining a fox's liver to cure a royal princess. In reward for kindness once shown by this lady to the foxes, the fox-wife brings her husband's liver in a basket, and places it at the foot of the princess's couch.

[1]Lecture delivered at the Philadelphia Polyclinic.

In our own times, the practice of seeking in the glands and viscera of animals for preparations of medicinal virtue has received a great impulse, almost to be termed a revival; first, through the experience of Brown-Séquard with testicular juice, then through that of British physicians with preparations of the thyroid gland, its greatest notoriety, however, being owing to the very recent publications of Ex-Surgeon-General Hammond.

In order that you may be able to follow the subject intelligently, let me, before going further, state the results; for which, afterward, I will give what appear to me to be the reasons.

Except in the hands of Brown-Séquard and his immediate colleagues, the injection of preparations of the testicles of animals has proved of very limited and uncertain therapeutic usefulness.

There is no testimony of which I am aware, other than that of Dr. Hammond in favor of the therapeutic virtue of that observer's "cerebrine" and "cardine."

Great therapeutic power has been demonstrated for preparations of the thyroid gland in the treatment of a certain group of disorders associated with diseases of the thyroid gland; namely, myxedema, cretinism and cachexia strumipriva; and more recently it has been said to be of use in the treatment of scaly diseases of the skin. It has proved of limited service in my hands, in a few cases, in the temporary relief of symptoms in exophthalmic-goiter and other forms of vasomotor ataxia, in diabetes mellitus, and in one case of akromegalia.

Preparations of the pancreas, aside from their well known benefit as digestive agents, have in the hands of Dr. Neville Wood, of Dr. Mansell, of Dr. Hector Mackenzie, and of others, including myself, proved useful, but not curative, in the treatment of certain cases of diabetes mellitus.

Preparations of the thymus gland have, in the hands of Dr. Charles Macalester of Liverpool, proved of great service in the treatment of pseudo-hypertrophic paralysis and general lymphadenoma, both of these being, as you will observe,

diseases of nutrition; diseases in which errors of metabolism are prominent features.

Preparations of nerve-tissue have been used by Gibier and others with varying results in epilepsy, in paralysis agitans, and in functional nervous disorders.

Here is the record of experience. Let us see what theory would indicate and compare our theoretic conclusions with these records.

Between such organs as, for example, the brain and the thyroid gland, there are many and great differences. One of these differences is all-important for the present discussion. The thyroid gland is a secretory organ; the brain is not. Without entering into a discussion of the exact nature of the process, concerning which the evidence is not clear, it is sufficient to know that clinical and experimental observations are at one in demonstrating that the thyroid gland manufactures some substance, which by its function in the economy, prevents the occurrence of the symptom-complexus termed myxedema or cachexia strumipriva; the former name being applied when the gland atrophies through disease, the latter when it has been removed by surgery.

Such being the case, it is natural to expect that if in cases in which defect or absence of the secretory functions of the thyroid gland has resulted in the development of these symptoms, we artificially supply the lacking secretion, the symptoms would disappear. The facts, as already stated, justify this expectation.

At first, the implantation of a thyroid gland in the abdomen was tried and proved successful with men and with animals. Later, Dr. Murray of Newcastle, England, injected subcutaneously preparations obtained by macerating the finely minced thyroid with glycerin, and still later, Hector Mackenzie and others showed that the administration of thyroid extract, of raw thyroid, and of dessicated thyroid by the mouth was equally efficacious.

The principle is exactly the same as that upon which we administer pepsin or pancreatin to replace the natural pep-

sin or pancreatin in digestive disorders; the body failing to furnish a certain substance which is necessary to the proper nutrition of all the organs, we supply that lack by administering a similar substance obtained from animals.

The mode of action, it is true, is somewhat different. The digestive ferments act locally in the stomach, that is outside the physiological interior of the body and upon foreign materials—food-stuffs. The thyroid preparations act within the blood or lymph after absorption, or if locally, upon the diseased tissues. The function of the gastric and pancreatic secretions in digestion is to prepare materials for nutrition; the function of the thyroid secretion is, probably, to destroy or antagonize certain products of function that otherwise act as toxines. In addition it prevents exaggerated growths of certain tissues. In a word, its function, as I have previously expressed it, is in truth "chemiotactic," that is inhibiting or regulatory in regard to the metabolic chemistry.

It will be observed, moreover, that whatever it may be that is accomplished by the administration of thyroid extract, it is not the cure of disease of the thyroid gland. No one, surely, expects to cure disease of the peptic glands by giving pepsin, or disease of the pancreas by giving pancreatin. It is the complex disorder resulting from the absence of thyroid secretion which is relieved in the one instance, just as it is the disorder caused by the absence of peptic or pancreatic secretion which is relieved in the other instances. In either instance there is no cure, for unless the administration of the thyroid preparation is kept up indefinitely, the symptoms due to the absence of thyroid secretion return just as the symptoms due to the absence of pepsin or pancreatin return when the administration of these drugs is stopped. Cure can only be obtained by measures which will secure natural reproduction of the missing secretions. So far as the thyroid gland is concerned we know, as yet, of no measure competent to effect this end.

Now, let us look at the other side of this question of animal extracts. The brain, so far as we know, secretes

nothing physical. So far as we know there is no symptom or symptom-complexus which can be attributed to defect in any supposed secretory function of the brain. Consequently, there is nothing in the whole nosology which on theoretic grounds, the administration of brain extract could be expected to remedy. Similarly, the heart so far as we know, secretes nothing and there is no symptom or symptom-complexus which can be attributed to default of supposed secretory function on the part of the heart. Equally, therefore, there is no ground for the administration of heart extract to remedy disorder caused by disease of that organ. For, let us remember, the thyroid extract does not cure thyroid disease, the thymus extract does not cure disease of the thymus, the pancreatic extract does not cure disease of the pancreas; and to expect brain extract to cure brain disease, or heart extract to cure heart disease, is on a par with the science of the Obi-doctor and the practice of the lizard-giving Chinamen.

This, however, does not exhaust the possibilities of the subject. Preparations of the tissues and juices of animals have a recognized place in the pharmacopeia. Thus, you are familiar with cantharidis and perhaps with blatta lapponica.

There is no reason, whatsoever, why the toxic and nutritive properties residing in substances of animal origin should not be utilized in medicine just as the toxic and nutritive properties residing in substances of vegetable and mineral origin are utilized. First, as to toxic properties: I say toxic properties, because while ordinarily we restrict the term toxic to effects which greatly disturb function or jeopardize life, yet, strictly speaking, every disturbance however slight, that is set up in the human economy by foreign substances, is a toxic effect, and it depends on the degree and character of that toxic effect whether the ultimate result is remedial or otherwise. The effect of atropin in paralyzing accommodation and causing mydriasis is, in suitable cases, therapeutically beneficial, but it is none the less the same in kind as the harmful effect that would

result from an overdose of the same drug.

There are many substances of animal origin, or that can be obtained by chemical manipulations of animal tissue, which possess the power of modifying the action of different organs and tissues of the human body; and I repeat, there is no reason whatsoever, why the properties of these substances should not be availed of in medicine. It needs only to be remembered that the particular organs or tissues from which such substances may be extracted bear no necessary relation to the organs affected in the diseases for the treatment of which these products may be employed. Thus, thyroid extract has a very decided diuretic power, and I have employed it with satisfaction, as a diuretic in a case of nephritis in a patient with no apparent disease of the thyroid gland.

Brain extract may, perhaps, prove to have beneficial action upon the heart or upon the kidneys; kidney extract may have a useful influence upon the organs of respiration; lung extract may have an hypnotic power. In other words, the true line of experimentation with animal extracts is the same as the true line of experimentation with drugs of mineral or vegetable origin. Their physiological or toxic powers should be studied in the laboratory and tested clinically without reference to their source; and only after such studies have been carefully made, can conclusions be drawn as to the probable usefulness in medical practice of the substances investigated.

And now, a word as to the nutritive properties of animal extracts. It may be that such extracts will afford a readily assimilable pabulum in diseases of certain tissues and organs, as we know such pabulum is furnished by preparations of phosphorus, iron, and other mineral substances found in the normal body, and by caffein and other vegetable products. Hence the injection of preparations of nerve-substance may have a rational basis. Again, it has been shown that certain important functions in resisting infection and in maintaining nutrition are performed by the nuclei of cells, and it may be that all animal extracts will

prove useful by virtue of the chemical constituents of the nucleus. This, too, is a proper field for clinical observation and laboratory experiment.

That the action of the thyroid gland in the treatment of myxedema is of an entirely different nature from either of these processes; that it is neither toxic nor, except in a very broad sense, nutritive;—that is, that while it regulates nutrition and prevents aberration of metabolism it is not directly used as a food element—I have already sufficiently explained. The action of the preparation of thyroid gland in relieving the headache of my case of akromegalia is possibly to be explained upon a somewhat different theory. The headache of akromegalia is due, at least in great part, to enlargement of the pituitary body. This enlargement of the pituitary body is probably supplementary to want of function on the part of the thyroid gland, the two being related embryologically. The administration of thyroid extract in this case may do away with the necessity of enlargement on the part of the pituitary body. But in a case in which the pituitary had already been enlarged sufficiently to produce permanent pressure symptoms, the administration of thyroid extract would not be expected to have any very decided result. In a mild case, where the process of enlargement was but beginning, it might be expected to hold that process in check. As to the effect of the thyroid extract in mitigating the general symptoms of akromegalia, experience is not yet sufficiently great to speak positively. I should expect it to act favorably in a recent case, and even in an old case to modify the progress of the disease. Of its effect in relieving headache in several cases of vasomotor disorder, and in one case of diabetes, and of its apparent temporary good effect in one case of exophthalmic goiter, I am not yet prepared to offer an explanation. The facts are worthy of record; beyond that, as yet, I cannot go. The doses used, which at all events are not dangerous in patients other than myxedematous, were from 10 to 15 grains of a dessicated preparation of sheep's thyroid gland made by Messrs Parke Davis & Co., and of which thirty grains represent an aver-

age gland. This was given once or twice daily, with aromatic powder, in hot beef-tea, or in hot coffee. The fact that similar doses could not be borne in myxedema, in which affection half a gland once a week seems to be effective, would indicate that in myxedema under the influence of the thyroid extract the abnormal tissues undergo chemical change, throwing into the circulation products that would be toxic if in great quantity, and hence must not be produced too rapidly for the excretory organs to deal with. In cases associated with cardiac lesion, absolute rest during treatment is said to be necessary; as two cases in which this precaution was neglected have proved fatal.

The administration of pancreatic extract in diabetes rests upon the experiments of Minkowsky, Lépine, and others who attribute a glycolytic function to some internal secretion of the pancreas. They found that when they had entirely extirpated the pancreas in certain animals, diabetes mellitus ensued; whereas, if a small portion of the pancreas were left, or if a pancreas graft had previously been successfully made beneath the skin of the abdomen, these symptoms either did not occur or were but transient. In this connection, we must remember that the mere secretion of sugar is but an incident in true diabetes, and as Harley has suggested, it is not alone deprivation of glycolytic ferment, but also the failure to remove or destroy certain excrementitious products ordinarily dealt with by the pancreas that renders the disease fatal. It is difficult, however, to determine clinically whether or not a given case of diabetes is of pancreatic origin. It is also as yet undetermined how much or how far in so-called pancreatic diabetes—that is, in cases that have exhibited pancreatic lesion post mortem, and in the experiments described—involvement of, or injury to the ganglia and nerves of the sympathetic system is responsible for the diabetic complexus of symptoms.

Thus while the administration of preparations of the pancreas by the stomach and hypodermatically is a legitimate expedient in any case of diabetes mellitus, and especially in cases associated with emaciation, we must not expect too

much from it.

In the case under observation at this hospital, we began with the injection twice daily of twenty minims of a specially prepared aseptic glycerin extract of the pancreas kindly manufactured for me by Messrs Parke, Davis & Co.; and we increased the dose up to forty minims twice daily. No bad local effect, such as digestion of the tissues or abscess, as I at first feared might be the case, was produced in a preliminary trial upon animals and upon himself, kindly made by our former resident physician, Dr. J. C. Knipe; and none resulted in our patient. The patient increased in weight and comfort; his skin became moister; his thirst diminished; and as less water was ingested less was excreted; but we observed no constant or decided effect upon the quantity of sugar excreted.

This, I believe, tallies with the experience of other observers. I have a case now under observation in private practice, in which improvement seems to have resulted through the administration of liquor pancreaticus by the mouth, but in this case also, the improvement is in the general condition of the patient and not in the excretion of sugar.

I have had but one experience with the Brown-Séquard fluid. Through the courtesy of my colleague, Professor Thomas S. K. Morton, I received from one who had received it direct from Brown-Séquard's laboratory a sealed packet of this preparation. I used it strictly according to the directions accompanying it, upon a patient at the Philadelphia Hospital, to whom the nature of the preparation and of the effects expected were explained. The patient was an intelligent man and welcomed the trial of the substance upon himself. The effect of suggestion was certainly not absent from the factors in the case. The result of the experiment, however, was *nil*. No improvement whatever resulted, although the case was a favorable one; debility without serious organic disease in a man of about sixty years of age.

To sum up, I would repeat my conclusions in the following form: Aside from their nutritive properties as general food or as food for special tissues, and aside from such anti-

septic power as may be due to the chemical constituents of cells or nuclei, preparations of animal organs and tissues may have, in the human body, action of one of two kinds, which may be termed respectively intrinsic and extrinsic; intrinsic, when they replace some normal secretion deficient in the patient; extrinsic, when they act as any other drug in modifying function and tissue without relation to the nature of the tissue from which they have been derived.

From Brown-Séquard's fluid, and possibly from Dr. Hammond's preparations, and others of like nature, effects of an extrinsic nature may be produced; but the effects of intrinsic nature can only be derived from preparations of secreting organs, that is, such preparations as thymus-extract, thyroid-extract, and pancreatic-extract. Even these latter, however, while they will have a large and extending field of usefulness in such diseases as anemia, lymphadenoma, rachitis, diabetes, myxedema, akromegaly and other errors of metabolism, do not and cannot cure diseases of the glands to remedy the deficiencies of which, they are administered.

To expect such action or to expect extract of brain to cure brain disease, extract of heart to cure heart disease, extract of kidney to cure kidney disease, is to desert the solid ground of experience and the steady light of science to follow into the bogs of mysticism the Jack-o'-lantern of savage superstition.

ACUTE INFLAMMATION OF THE LACHRYMAL SAC.

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The lachrymal sac is not unfrequently the seat of acute inflammation. A swelling appears at the inner angle of the eye near the root of the nose, immediately beneath the internal palpebral ligament; the tumor is irregular in outline, not sharply defined, very painful and sensitive to pressure;